



General

Guideline Title

Final recommendation statement: hormone therapy in postmenopausal women: primary prevention of chronic conditions.

Bibliographic Source(s)

Final recommendation statement: hormone therapy in postmenopausal women: primary prevention of chronic conditions. [internet]. Rockville (MD): U.S. Preventive Services Task Force (USPSTF); 2017 Dec [10 p]. [40 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force. Menopausal hormone therapy for the primary prevention of chronic conditions: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2013 Jan 1;158(1):47-54.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report [Clinical Practice Guidelines We Can Trust](#).

■■■■■= Poor ■■■■■= Fair ■■■■■= Good ■■■■■= Very Good ■■■■■= Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
■■■■■	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
■■■■	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
■■■■■	Search Strategy
■■■■■	Study Selection
■■■■■	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
■■■■■	Grading the Quality or Strength of Evidence
■■■■■	Benefits and Harms of Recommendations
■■■■■	Evidence Summary Supporting Recommendations
■■■■■	Rating the Strength of Recommendations
■■■■■	Specific and Unambiguous Articulation of Recommendations
■■■■■	External Review
■■■■■	Updating

Recommendations

Major Recommendations

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and identifies the levels of certainty regarding net benefit (High, Moderate, and Low). The definitions of these grades can be found at the end of the "Major Recommendations" field.

Recommendation Summary

The USPSTF recommends against the use of combined estrogen and progestin for the primary prevention of chronic conditions in postmenopausal women. (D recommendation)

The USPSTF recommends against the use of estrogen alone for the primary prevention of chronic conditions in postmenopausal women who have had a hysterectomy. (D recommendation)

Clinical Considerations

Patient Population Under Consideration

This recommendation statement applies to asymptomatic, postmenopausal women who are considering hormone therapy for the primary prevention of chronic medical conditions. It does not apply to women

who are considering hormone therapy for the management of menopausal symptoms, such as hot flashes or vaginal dryness. It also does not apply to women who have had premature menopause (primary ovarian insufficiency) or surgical menopause.

Assessment of Risk

This recommendation statement applies to an average-risk population. Risk factors for a specific chronic condition or individual characteristics that affect the likelihood of experiencing a specific therapy-associated adverse event may cause a woman's net balance of benefits and harms to differ from that of the average population.

Treatment and Intervention

Menopausal hormone therapy refers to the use of combined estrogen and progestin in women with an intact uterus, or estrogen alone in women who have had a hysterectomy, taken at or after the time of menopause. For this recommendation, the USPSTF considered evidence on the benefits and harms of systemic (i.e., oral or transdermal) menopausal hormone therapy but not local formulations (e.g., creams or rings) of hormone therapy, because these are not generally used for the primary prevention of chronic conditions.

Indications for hormone therapy approved by the U.S. Food and Drug Administration (FDA) in menopausal women are limited to the treatment of menopausal symptoms and the prevention of postmenopausal osteoporosis. An FDA-issued black box warning indicates that estrogen therapy, with or without progestin, should be prescribed at the lowest effective dose and for the shortest duration consistent with the patient's treatment goals and risks.

Several different formulations of menopausal hormone therapy are approved by the FDA for use in the United States; the specific formulation used in the Women's Health Initiative (WHI) trial, the largest trial reviewed by the USPSTF, was 0.625 mg/d of oral conjugated equine estrogens, with or without 2.5 mg/d of medroxyprogesterone acetate. Currently, evidence to determine whether different types, doses, or modes of delivery of hormone therapy affect its benefit-to-harm profile for the prevention of chronic conditions is limited.

The use of menopausal hormone therapy is associated with both benefits and harms. Combined estrogen and progestin use is associated with a decreased risk of fractures, diabetes, and colorectal cancer; however, it is also associated with an increased risk of invasive breast cancer, coronary heart disease, thromboembolic events, stroke, dementia, gallbladder disease, and self-reported urinary incontinence. Estrogen use alone is associated with a decreased risk of fractures, invasive breast cancer, and diabetes; however, it is also associated with an increased risk of thromboembolic events, stroke, dementia, gallbladder disease, and self-reported urinary incontinence. The reason for the discordant effect of estrogen alone compared with combined estrogen and progestin on the risk of invasive breast cancer is unclear. Table 1 and Table 2 in the original guideline document show the estimated absolute event rate differences associated with the use of combined estrogen and progestin and estrogen alone, compared with placebo, for these health outcomes.

Other Approaches to Prevention

Several interventions and preventive medications to reduce the risk of chronic conditions in women have been studied. For example, the use of medications such as tamoxifen and raloxifene in women at increased risk of breast cancer who do not have contraindications and are at low risk of adverse medication effects is a potential strategy to reduce risk of breast cancer. The USPSTF recommends behavioral counseling interventions to promote a healthful diet and physical activity for the prevention of cardiovascular disease in adults who are overweight or obese and have additional cardiovascular disease risk factors. The USPSTF also recommends daily use of low-dose aspirin to decrease the risk of colorectal cancer and cardiovascular disease in appropriate candidates.

Definitions

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the "Clinical Considerations" section of the USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	<p>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:</p> <ul style="list-style-type: none"> The number, size, or quality of individual studies Inconsistency of findings across individual studies Limited generalizability of findings to routine primary care practice Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> The limited number or size of studies Important flaws in study design or methods Inconsistency of findings across individual studies Gaps in the chain of evidence Findings not generalizable to routine primary care practice A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Chronic conditions including:

- Coronary heart disease
- Breast cancer, colorectal cancer, and other types of cancer
- Thromboembolic events such as venous thromboembolism
- Stroke
- Cognitive Impairment such as dementia
- Gallbladder disease
- Urinary Incontinence
- Fractures
- Diabetes

Guideline Category

Prevention

Clinical Specialty

- Family Practice
- Internal Medicine
- Obstetrics and Gynecology
- Preventive Medicine

Intended Users

- Advanced Practice Nurses
- Allied Health Personnel
- Health Care Providers
- Nurses
- Physician Assistants
- Physicians

Guideline Objective(s)

To update the 2012 U.S. Preventive Services Task Force (USPSTF) recommendation statement on hormone therapy for the prevention of chronic conditions in postmenopausal women

Target Population

Asymptomatic, postmenopausal women who are considering hormone therapy for the primary prevention of chronic medical conditions

Note: These recommendations do not apply to women who are considering hormone therapy for the management of menopausal symptoms, such as hot flashes or vaginal dryness. It also does not apply to women who have had premature menopause (primary ovarian insufficiency) or surgical menopause.

Interventions and Practices Considered

Hormone therapy:

- Combined estrogen and progestin (considered but not recommended)
- Estrogen alone (considered but not recommended)

Major Outcomes Considered

- Key Question 1: What are the benefits of menopausal hormone therapy when used for the primary prevention of chronic conditions?
- Key Question 2: What are the harms of menopausal hormone therapy when used for the primary prevention of chronic conditions?
- Key Question 3: Do the benefits and harms of menopausal hormone therapy differ by subgroup (race/ethnicity; women with premature menopause; women with surgical menopause; age during hormone therapy use; duration of use; type, dose, and mode of delivery of hormone therapy; and presence of comorbid conditions) or by timing of intervention (initiation of hormone therapy during perimenopause vs. postmenopause)?

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the RTI International–University of North Carolina Evidence-based Practice Center (EPC) for use by the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Search Strategies

The EPC staff searched MEDLINE® (via PubMed), the Cochrane Library, EMBASE, and International Pharmaceutical Abstracts for English-language articles published from June 1, 2011, through August 1, 2016. They used Medical Subject Headings as search terms when available and keywords when appropriate, focusing on terms to describe relevant PICOTS elements. Appendix A of the systematic review describes all the search strategies.

The EPC staff conducted targeted searches for unpublished literature by searching ClinicalTrials.gov, HSRProj, the World Health Organization's International Clinical Trials Registry Platform, NIH RePORTER,

and Drugs@FDA.gov. To supplement electronic searches, they reviewed the reference lists of pertinent review articles and studies meeting our inclusion criteria and added all previously unidentified relevant articles. They also manually reviewed all literature suggested by peer reviewers or public comment respondents and, if appropriate, incorporated it into the final review.

Between August 2016 and August 2017, they conducted ongoing surveillance through article alerts and targeted searches of high-impact journals to ensure inclusion of major studies affecting the conclusions or understanding of the evidence and the related USPSTF recommendation.

Study Selection

The EPC staff selected hormone therapy studies on the basis of inclusion and exclusion criteria developed for each key question (KQ) based on the population, intervention, comparator, outcome, time, setting (PICOTS) approach and other elements such as study designs. The basic criteria are described below, and Appendix B of the systematic review provides more details. All citations identified through searches and other sources were imported into EndNote Version 7 (Clarivate Analytics, Philadelphia).

Two investigators independently reviewed titles and abstracts. They then dually and independently reviewed the full text of all articles that either reviewer marked for potential inclusion. Disagreements were resolved by discussion and consensus; if necessary, they sought adjudication of conflicts from other experienced members of the review team. Appendix E of the systematic review lists studies that were excluded at the full-text review stage.

In addition to the searches for the updated literature, they incorporated all included citations from the previous report, which covered the publication period of January 2002 through November 2011. Additionally, to ensure that the update was cumulative of all relevant evidence, they reviewed all included citations from three recent systematic reviews and included all relevant citations that met the criteria for fair or good quality.

Number of Source Documents

The update identified 2,241 citations. Of these, 1,989 abstracts were excluded and investigators reviewed 252 full-text articles. Of these, 17 articles reporting on 13 trials that met inclusion criteria were retained. Overall, 68 articles from the previous review and this update represented a total of 18 good- or fair-quality trials. Appendix D of the systematic review (see the "Availability of Companion Documents" field) documents the disposition of the articles identified from searches (i.e., the flowchart of the literature). Appendix E lists articles excluded at full-text review.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Using predefined criteria developed by the U.S. Preventive Services Task Force (USPSTF) two investigators independently assessed the quality of each study as good, fair, or poor. The USPSTF criteria are listed in Appendix C of the systematic review (see the "Availability of Companion Documents" field). Appendix F lists the ratings for each domain for each eligible study. Disagreements were resolved by discussion and consensus.

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the RTI International–University of North Carolina Evidence-based Practice Center (EPC) for use by the U.S. Preventive Services Task Force (USPSTF); see the "Availability of Companion Documents" field.

Data Extraction and Quality Rating

An investigator abstracted pertinent information from each included study; details included methods and the PICOTS elements. A second investigator checked all data abstractions for completeness and accuracy. Differences were resolved by consensus or adjudication by a third senior investigator.

Using predefined criteria developed by the USPSTF, two investigators independently assessed the quality of each study as good, fair, or poor. Disagreements were resolved by discussion and consensus. Trials with fatal flaws were rated as poor quality (i.e., high risk of bias). Fatal flaws that resulted in poor-quality ratings included initially assembled groups that were not close to being comparable or were not maintained throughout the study, overall attrition of at least 20 percent or differential attrition of at least 15 percentage points between groups, and use of unreliable or invalid measurement instruments or unequal application among groups (including not masking outcome assessment). For randomized controlled trials (RCTs), the lack of intention-to-treat analysis was also a reason for rating a trial as poor quality.

Data Synthesis and Analysis

The investigators qualitatively synthesized findings for each key question (KQ) by summarizing the characteristics and results of included studies in tabular or narrative format. To determine whether meta-analyses were appropriate, they assessed both the number of trials available and their clinical and methodological heterogeneity following established guidance. To do this, they qualitatively assessed the populations, similarities and differences in treatments used, and similarities in outcomes and timing of outcomes assessed.

When at least three similar trials were available, they conducted quantitative synthesis of studies with random-effects models using the inverse-variance weighted method (DerSimonian and Laird).

For all quantitative syntheses, investigators calculated the chi-squared statistic and the I^2 statistic (the proportion of variation in study estimates attributable to heterogeneity rather than due to chance) to assess statistical heterogeneity in effects between studies. An I^2 from 0 to 40 percent might not be important, 30 to 60 percent may represent moderate heterogeneity, 50 to 90 percent may represent substantial heterogeneity, and 75 percent or greater represents considerable heterogeneity. The importance of the observed value of I^2 depends on the magnitude and direction of effects and on the strength of evidence (SOE) for heterogeneity (e.g., p-value from the chi-squared test or a confidence interval [CI] for I^2). However, as precision and the number of subjects increase, I^2 may become inflated toward 100 percent and may not reflect clinically relevant heterogeneity.

All the quantitative analyses were conducted using Comprehensive Meta-Analysis Version 3 (Biostat, Englewood, NJ).

The SOE was rated for each major outcome for each KQ using the domains set out in the AHRQ guidance: study limitations, consistency, precision, directness, and reporting bias. Other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, and strength of association (magnitude of effect) were also considered.

Two reviewers assessed each SOE domain for each key outcome and developed the overall SOE grades. The reviewers were two senior members of the review team (including at least one subject matter expert

and one methodologist); they resolved any differences by consensus discussion.

SOE grades reflect the confidence that the reviewers have that various estimates of effect are close to true effects with respect to the KQs in a systematic review. A high grade indicates confidence that the estimate of effect lies close to the true effect for this outcome, the body of evidence has few or no deficiencies, and the findings are stable. A moderate grade suggests that although the estimate of effect lies close to the true effect for this outcome, the body of evidence has some deficiencies, and some doubt persists as to the stability of the findings. A low grade suggests limited confidence about the estimate of effect, with the need for additional studies. Insufficient evidence means that the reviewers have no evidence, are unable to estimate an effect, or have no confidence in the estimate of effect for this outcome.

Methods Used to Formulate the Recommendations

Balance Sheets

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The U.S. Preventive Services Task Force (USPSTF) systematically reviews the evidence concerning both the benefits and harms of widespread implementation of a preventive service. It then assesses the certainty of the evidence and the magnitude of the benefits and harms. On the basis of this assessment, the USPSTF assigns a letter grade to each preventive service signifying its recommendation about provision of the service (see table below). An important, but often challenging, step is determining the balance between benefits and harms to estimate "net benefit" (that is, benefits minus harms).

U.S. Preventive Services Task Force Recommendation Grid*

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	Insufficient			

*A, B, C, D, and I (*Insufficient*) represent the letter grades of recommendation or statement of insufficient evidence assigned by the USPSTF after assessing certainty and magnitude of net benefit of the service (see the "Rating Scheme for the Strength of the Recommendations" field).

The overarching question that the USPSTF seeks to answer for every preventive service is whether evidence suggests that provision of the service would improve health outcomes if implemented in a general primary care population. For screening topics, this standard could be met by a large randomized controlled trial (RCT) in a representative asymptomatic population with follow-up of all members of both the group "invited for screening" and the group "not invited for screening."

Direct RCT evidence about screening is often unavailable, so the USPSTF considers indirect evidence. To guide its selection of indirect evidence, the USPSTF constructs a "chain of evidence" within an analytic framework. For each key question, the body of pertinent literature is critically appraised, focusing on the following 6 questions:

- Do the studies have the appropriate research design to answer the key question(s)?
- To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
- To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
- How many studies have been conducted that address the key question(s)? How large are the

studies? (i.e., what is the precision of the evidence?)

How consistent are the results of the studies?

Are there additional factors that assist the USPSTF in drawing conclusions (e.g., presence or absence of dose-response effects, fit within a biologic model)?

The next step in the USPSTF process is to use the evidence from the key questions to assess whether there would be net benefit if the service were implemented. In 2001, the USPSTF published an article that documented its systematic processes of evidence evaluation and recommendation development. At that time, the USPSTF's overall assessment of evidence was described as good, fair, or poor. The USPSTF realized that this rating seemed to apply only to how well studies were conducted and did not fully capture all of the issues that go into an overall assessment of the evidence about net benefit. To avoid confusion, the USPSTF has changed its terminology. Whereas individual study quality will continue to be characterized as good, fair, or poor, the term *certainty* will now be used to describe the USPSTF's assessment of the overall body of evidence about net benefit of a preventive service and the likelihood that the assessment is correct. Certainty will be determined by considering all 6 questions listed above; the judgment about certainty will be described as high, moderate, or low.

In making its assessment of certainty about net benefit, the evaluation of the evidence from each key question plays a primary role. It is important to note that the USPSTF makes recommendations for real-world medical practice in the United States and must determine to what extent the evidence for each key question—even evidence from screening RCTs or treatment RCTs—can be applied to the general primary care population. Frequently, studies are conducted in highly selected populations under special conditions. The USPSTF must consider differences between the general primary care population and the populations studied in RCTs and make judgments about the likelihood of observing the same effect in actual practice.

It is also important to note that one of the key questions in the analytic framework refers to the potential harms of the preventive service. The USPSTF considers the evidence about the benefits and harms of preventive services separately and equally. Data about harms are often obtained from observational studies because harms observed in RCTs may not be representative of those found in usual practice and because some harms are not completely measured and reported in RCTs.

Putting the body of evidence for all key questions together as a chain, the USPSTF assesses the certainty of net benefit of a preventive service by asking the 6 major questions listed above. The USPSTF would rate a body of convincing evidence about the benefits of a service that, for example, derives from several RCTs of screening in which the estimate of benefits can be generalized to the general primary care population as "high" certainty (see the "Rating Scheme for the Strength of Recommendations" field). The USPSTF would rate a body of evidence that was not clearly applicable to general practice or has other defects in quality, research design, or consistency of studies as "moderate" certainty. Certainty is "low" when, for example, there are gaps in the evidence linking parts of the analytic framework, when evidence to determine the harms of treatment is unavailable, or when evidence about the benefits of treatment is insufficient. Table 4 in the methodology document listed below (see the "Availability of Companion Documents" field) summarizes the current terminology used by the USPSTF to describe the critical assessment of evidence at all 3 levels: individual studies, key questions, and overall certainty of net benefit of the preventive service.

Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. *Ann Intern Med*. 2007;147:871-875.[5 references].

Rating Scheme for the Strength of the Recommendations

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There	Offer or provide this service.

Grade	Grade Definitions	Suggestions for Practice
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	<p>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:</p> <ul style="list-style-type: none"> The number, size, or quality of individual studies Inconsistency of findings across individual studies Limited generalizability of findings to routine primary care practice; and Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> The limited number or size of studies Important flaws in study design or methods Inconsistency of findings across individual studies Gaps in the chain of evidence Findings that are not generalizable to routine primary care practice; and A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Cost Analysis

The U.S. Preventive Services Task Force (USPSTF) does not consider the costs of providing a service in

this assessment.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Peer Review

Before the U.S. Preventive Services Task Force (USPSTF) makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft evidence review to 4 to 6 external experts and to Federal agencies and professional and disease-based health organizations with interests in the topic. The experts are asked to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. The draft evidence review is also posted on the USPSTF Web site for public comment. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the USPSTF in memo form. In this way, the USPSTF can consider these external comments before it votes on its recommendations about the service. Draft recommendation statements are then circulated for comment among reviewers representing professional societies, voluntary organizations, and Federal agencies, as well as posted on the USPSTF Web site for public comment. These comments are discussed before the final recommendations are confirmed.

Responses to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from May 16 to June 12, 2017. In response to public comment, the USPSTF modified the title of the recommendation statement to clarify that the patient population under consideration consists of postmenopausal women. The USPSTF clarified that it reviewed the evidence on the benefits and harms of systemic menopausal hormone therapy (i.e., administered orally or transdermally), not local hormone therapy (e.g., creams or rings). The USPSTF also provided additional details about the Women's Health Initiative (WHI) trial, specifying the formulation of hormone therapy used and the average age of women enrolled in the trial. The USPSTF added 2 tables (see Tables 1 and 2 in the original guideline document) showing the absolute risk increase or decrease of various health outcomes in women receiving combined estrogen and progestin or estrogen alone.

In response to comments that some subgroups of women (e.g., women aged 50 to 59 years taking estrogen alone) experience a more beneficial balance of benefits and harms than the overall group of women in the WHI trial, the USPSTF expanded its discussion on the interaction between age and health outcomes in the WHI trial in the "Discussion" section. The USPSTF also clarified that the WHI analyses that assessed whether time between menopause and initiation of hormone therapy affects the benefits and harms of hormone therapy were conducted post hoc.

The USPSTF added the word "primary" to the recommendation summary to further highlight that this recommendation statement focuses on the use of hormone therapy for the primary prevention of chronic conditions in postmenopausal women, not on its use for the treatment of vasomotor, vulvovaginal, or other symptoms. The USPSTF is tasked with evaluating the benefits and harms of clinical preventive services in generally asymptomatic populations; therefore, the treatment of symptoms is outside of its purview.

The USPSTF agrees with comments regarding the importance of individualized and shared decision

making, and states so in the preamble to each recommendation statement. Last, the USPSTF clarified the definition of menopause in the "Rationale" section and added a reference to the Endocrine Society's guidelines on hormone therapy in the "Recommendations of Others" section in the original guideline document.

Comparison with Guidelines from Other Groups

Recommendations for hormone therapy in postmenopausal women for the primary prevention of chronic conditions from the following groups were discussed: The American Heart Association, the American College of Obstetricians and Gynecologists, the Canadian Task Force on Preventive Health Care, the American Academy of Family Physicians, the American Association of Clinical Endocrinologists, the North American Menopause Society, and the Endocrine Society.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Combined Estrogen and Progestin

Many health outcomes potentially associated with the use of hormone therapy in postmenopausal women have been examined. The U.S. Preventive Services Task Force (USPSTF) found convincing evidence that use of combined estrogen and progestin has a moderate benefit in reducing the risk of fractures in postmenopausal women and adequate evidence that it has a small benefit in reducing the risk of diabetes.

Estrogen Alone

The use of estrogen without progestin has generally been restricted to women who have had a hysterectomy, because unopposed estrogen use increases the risk of endometrial cancer in women with an intact uterus. The USPSTF found convincing evidence that use of estrogen alone has a moderate benefit in reducing the incidence of fractures in postmenopausal women. The USPSTF found adequate evidence that the use of estrogen alone has a moderate benefit in reducing the risk of developing or dying of invasive breast cancer and a small benefit in reducing the risk of diabetes. The USPSTF found convincing evidence that estrogen use does not have a beneficial effect on risk of coronary heart disease.

Potential Harms

Combined Estrogen and Progestin

The U.S. Preventive Services Task Force (USPSTF) found convincing evidence that use of combined estrogen and progestin is associated with moderate harms, including increased risk of invasive breast cancer and venous thromboembolism, and a small to moderate harm of increased risk of coronary heart disease. The USPSTF also found adequate evidence of other moderate harms, such as increased risk of stroke, dementia, gallbladder disease, and urinary incontinence.

Estrogen Alone

The USPSTF found adequate evidence that use of estrogen alone is associated with moderate harms, including increased risk of stroke, dementia, gallbladder disease, urinary incontinence, and venous thromboembolism.

Qualifying Statements

Qualifying Statements

- The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.
- It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.
- The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.
- Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Implementation of the Guideline

Description of Implementation Strategy

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the USPSTF will make all its products available through its [Web site](#) . The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access USPSTF materials and adapt them for their local needs. Online access to USPSTF products also opens up new possibilities for the appearance of the annual, pocket-size *Guide to Clinical Preventive Services*.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal

with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

Implementation Tools

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Final recommendation statement: hormone therapy in postmenopausal women: primary prevention of chronic conditions. [internet]. Rockville (MD): U.S. Preventive Services Task Force (USPSTF); 2017 Dec [10 p]. [40 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Dec

Guideline Developer(s)

U.S. Preventive Services Task Force - Independent Expert Panel

Guideline Developer Comment

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services (DHHS) or DHHS agencies.

Source(s) of Funding

The U.S. Preventive Services Task Force (USPSTF) is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

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U.S. Preventive Services Task Force (USPSTF)

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**Members of the USPSTF at the time this recommendation was finalized. For a list of current Task Force members, go to <https://www.uspreventiveservicestaskforce.org/Page/Name/our-members> .*

Financial Disclosures/Conflicts of Interest

The U.S. Preventive Services Task Force (USPSTF) has an explicit policy concerning conflict of interest. All members disclose at each meeting if they have a significant financial, professional/business, or intellectual conflict for each topic being discussed. USPSTF members with conflicts may be recused from discussing or voting on recommendations about the topic in question.

Conflict of Interest Disclosures

All authors have completed and submitted the International Committee of Medical Journal Editors (ICMJE) Form for Disclosure of Potential Conflicts of Interest. Authors followed the policy regarding conflicts of interest described at <https://www.uspreventiveservicestaskforce.org/Page/Name/conflict-of-interest-disclosures> . All members of the USPSTF receive travel reimbursement and an honorarium for participating in USPSTF meetings.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force. Menopausal hormone therapy for the primary prevention of chronic conditions: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2013 Jan 1;158(1):47-54.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .

Availability of Companion Documents

The following are available:

Evidence Reviews:

Gartlehner G, Patel SV, Feltner C, Weber RP, Long R, Mullican K, Boland E, Lux L, Viswanathan M. Hormone therapy for the primary prevention of chronic conditions in postmenopausal women: evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2017;318(22):2234-49

Gartlehner G, Patel SV, Viswanathan M, Feltner C, Weber RP, Lee R, Mullican K, Boland E, Lux L, Lohr K. Hormone therapy for the primary prevention of chronic conditions in postmenopausal women: an evidence review for the U.S. Preventive Services Task Force. Evidence synthesis no. 155. AHRQ publication no. 15-05227-EF-1. Rockville (MD): Agency for Healthcare Research and Quality; 2017 Dec.

Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .

The following is also available:

Hormone therapy in postmenopausal women: primary prevention of chronic conditions. Clinical summary. Rockville (MD): U.S. Preventive Services Task Force; 2017 Dec. Available from the [USPSTF Web Site](#) .

The [Electronic Preventive Services Selector \(ePSS\)](#) , available as a PDA application and a web-based tool, is a quick hands-on tool designed to help primary care clinicians identify the screening, counseling, and preventive medication services that are appropriate for their patients. It is based on current recommendations of the USPSTF and can be searched by specific patient characteristics such as age, sex, and selected behavioral risk factors.

Patient Resources

Myhealthfinder is a tool that provides personalized recommendations for clinical preventive services specific to the user's age, gender, and pregnancy status. It features evidence-based recommendations from the USPSTF and is available at [www.healthfinder.gov](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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